

ORAL PRESENTATION

Open Access

Roles of *COMT*, *NPY* and *GCH1* in acute and chronic pain/stress response

David Goldman

From Seventh Scientific Meeting of The TMJ Association, Genetic, Epigenetic, and Mechanistic Studies of Temporomandibular Disorders and Overlapping Pain Conditions
Bethesda, MD, USA. 7-9 September 2014

Pain is a pervasive stressor often experienced chronically, and strongly modulated by the brain's emotional circuitry. In recent years functional polymorphisms at several genes have been linked to pain response, encouraging the idea that both pain response and other aspects of emotionality can be better understood by genetic studies of acute and chronic pain, as illustrated by studies performed with several genes, two of which also alter anxiety and emotional responses. The functional *COMT* Val158Met locus, which had been tied to frontal cognitive function, trait anxiety and brain metabolic responses to emotional stimuli, was linked to the ability of acute pain to release endomorphin and displace ^{11}C carfentanil binding following a pain challenge [1]. The anxiety-associated Met158 allele predicts both lower pain threshold and stronger affective response to pain. This finding was replicated in a large sample of women prospectively followed or temporomandibular joint pain and measured for experimental pain (Diatchenko et al). These investigators later showed that the *COMT* haplotype linkage is better understood via the epistatic interaction of alleles to alter translatability of *COMT* mRNA. GTP cyclohydrolase (*GCH1*) represents a second gene influencing pain (Tegeder et al, *Nat Neuroscience*). The gene was identified as a candidate via array expression in the rat neurotomy model. In humans, a functional haplotype predicting *GCH1* mRNA expression in lymphoblastoid cell lines. Consistent with the rat data, the high expression diplotype was linked to both clinical post lumbar surgery leg pain and to experimental pain in a large population of controls. Continuing the theme that genes that alter emotion can also alter pain responses, a functional polymorphism in the *NPY* (neuropeptide Y) promoter alters both amygdala and hippocampal emotional

responses as well as predicting ^{11}C carfentanil displacement after a pain challenge [2].

Published: 15 December 2014

References

1. Zubieta JK, Heitzeg MM, Smith YR, Bueller JA, Xu K, Xu Y, Koeppe RA, Stohler CS, Goldman D: **COMT val158met genotype affects mu-opioid neurotransmitter responses to a pain stressor.** *Science* 2003, **299**(5610):1240-3.
2. Zhou Z, Zhu G, Hariri AR, Enoch MA, Scott D, Sinha R, Virkkunen M, Mash DC, Lipsky RH, Hu XZ, Hodgkinson CA, Xu K, Buzas B, Yuan Q, Shen PH, Ferrell RE, Manuck SB, Brown SM, Hauger RL, Stohler CS, Zubieta JK, Goldman D: **Genetic variation in human NPY expression affects stress response and emotion.** *Nature* 2008, **452**(7190):997-1001.

doi:10.1186/1744-8069-10-S1-O5

Cite this article as: Goldman: Roles of *COMT*, *NPY* and *GCH1* in acute and chronic pain/stress response. *Molecular Pain* 2014 **10**(Suppl 1):O5.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit



Laboratory of Neurogenetics, NIAAA, Rockville, MD 20852, USA



© 2014 Goldman; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.